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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,483	03/29/2004	Jun Liu	P2026R1	5594

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GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
KIM, YUNSOO	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/813,483	LIU ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8,16-25,28-45 and 48-50* is/are pending in the application.

4a) Of the above claim(s) *18,19,21,28-45,48-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-8,16,17,20,22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/28/06,9/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 3-8, 16-25, 28-45 and 48-50 are pending.

Claims 18, 19, 21, 28-45 and 48-50 remain withdrawn from further consideration by examiner 37 CFR.1.142(b) as being drawn to a nonelected species.

Claims 1, 3-8, 16, 17, 20 and 22-25 are under consideration.

2. In view of Applicants' amendment to the claims, the following rejections remain.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 3-8 and 20 stand rejected under 35 U.S.C. 102(e) as being anticipated by US2003/0138417 A1, of record as is evidenced by the US 2004/0191243A1, newly cited for the reasons set forth in the office action mailed 4/3/06.

The '417 publication teaches a stable isotonic liquid pharmaceutical antibody formulation comprising 50mM histdine buffer, 0.03% polysorbate at pH 6 (Example 8, [104], in particular). The '417 publication further teaches that the pharmaceutical antibody formulation can be used in stabilizing antibody including IgE monoclonal antibody ([0039-42], in particular) at concentration greater than 100 mg/ml (abstract, claims 2-3, in particular) with about 50-200mM of tonicity modifier such as arginine ([0052], in particular).

In addition, the '417 publication teaches that the isotonic means having osmotic pressure from.270-328 mOsm ([0029], in particular). Moreover, the highly concentrated stable antibody formulation taught in the '417 publication is suitable for various methods of administration, prevents aggregations and increase storage time ([0003], [0013-15], in particular).

Thus, having low turbidity and kinematic viscosity about 50cs are inherent property of antibody formulation comprising 50 mM Histidine buffer at pH. 6, about 50-200 mM arginine and 0.03% of polysorbate. Therefore, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 9/21/06 have been fully considered but they were not persuasive.

Applicants traversed the rejection based on that there is no specific guidance as in the '417 publication to select arginine-HCl as a tonicity modifier and the examples disclosed in the '417 publication are not enabling.

Contrary to Applicants' arguments, it is well known in the art as is evidenced by the '243 publication on p. 10-11, ([100, 105], and on p. 10, Table 5, in particular) that the arginine has been used in histidine buffer containing formulations for reduced viscosity.

Applicants further traversed that the presence of NaCl does not result the reduction of viscosity and the examples of '417 publication are not enabling. However, the presence of NaCl is not the claimed subject matter and the '417 publication specifically teaches that the above pharmaceutical formulation is suitable for stabilizing antibody concentration greater than 100mg/ml (claims 2-3, in particular). Thus, the reference teachings anticipate the claimed invention.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 16, 17, 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US2003/0138417 (of record) as is evidenced by the US 2004/109243A1, newly cited, in view of U.S. Pat. No. 5,994,511 (IDS reference, of record) for the reasons set forth in the office action mailed 4/3/06.

Applicants' arguments filed 9/21/06 have been fully considered but they were not persuasive.

Applicants traversed the rejection based on that the '417 publication is not anticipatory reference and the combination of teachings is not obvious.

In light of the discussion above in sections 3-4, the '417 publication is a proper anticipatory reference and the combination of teachings remains obvious.

7. The following new grounds of rejection are necessitated by the Applicants' submission of supplemental IDS filed 7/28/06 and 9/21/06.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 3-8, 16, 17, 20 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/26909, IDS reference, in view of U.S. Pat. No. 5,994,511 (IDS reference, of record).

The '909 publication teaches a stable protein formulation comprising 10 mM histidine,160 mM arginine-HCl at pH. 7, protein concentration of about 160mg/ml and 0.05% of polysorbate (claims 1-49, in particular).

The '909 publication further teaches that the stable protein formulation adds stability to the protein and enhances therapeutic applicability (p. 5, in particular).

Claims 4-5 are included in this rejection because the concentrations of 180mg/ml or 200 mg/ml are well within the purview of optimization of about 160mg/ml.

In addition, having low turbidity, kinematic viscosity about 50cs and having osmotic pressure from 270-328 mOsm are inherent property of the protein formulation comprising 10 mM histidine,16 mM arginine-HCl at pH. 7 and 0.05% of polysorbate.

The '909 publication does not teach rhuMabE25 as in claims 16 and 17, article or manufacture with syringe or injection device as in claims 22-25.

However, the '511 patent teaches rhuMabE25 (Table 1, claims 9-10, in particular) composition and an article of manufacture comprising syringes or injection tools (col. 58-59 overlapping paragraph, in particular).

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to stabilize rhuMabE25 as taught by the '511 patent with a formulation comprising a buffer comprising histidine, arginine and polysorbate as taught by the '909 publication.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the '909 publication teaches that a formulation comprising histidine, arginine and polysorbate adds stability to any antibodies and prevents degradation proteins (p. 5, in particular).

From the teachings of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1, 3-8, 16, 17, 20 and 22-25 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7-13, 22-27, 31-34, 37-42, 48, 51-56, 58 and 59 of U.S. Patent No. 6,875,432 B2 in view of US 2004/109243A1.

The '432 patent teaches a stable antibody formulation comprising about 80- about 130mg/ml of rhuMab E25 (or 2-40 times higher when reconstituted), histidine buffer, arginine-HCl and polysorbate (claims 1-4, 7-13, 22-27, 31-34, in particular). The '432 patent further teaches that the stable formulation has viscosity less than 50cs and an article of manufature (claims 37-42, 48 and 58-59, in particular).

The '432 patent does not recite particular concentration ranges of histidine, arginine and polysorbate.

However, the '243 publication teaches a particular range of histidine being 10-50mM, arginine-HCl being about 60mM and the polysorbate at 0.01 to 0.1% (Table 5, [0094-0105], in particular) and it is well known in the art that addition of arginine in combination of histidine decreases viscosity ([105], in particular).

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to use the concentration ranges of the components of the stabilizing formulation as taught by the '243 publication in the stabilizing formulation comprising a buffer comprising histidine, arginine and polysorbate as taught by the '909 publication.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the known concentration ranges of the '243 publication reduce undue optimization the stabilizing formulation while reducing solution viscosity.

From the teachings of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claims are allowable.

13. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 9/21/06 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yunsoo Kim
Patent Examiner
Technology Center 1600
December 14, 2006

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600